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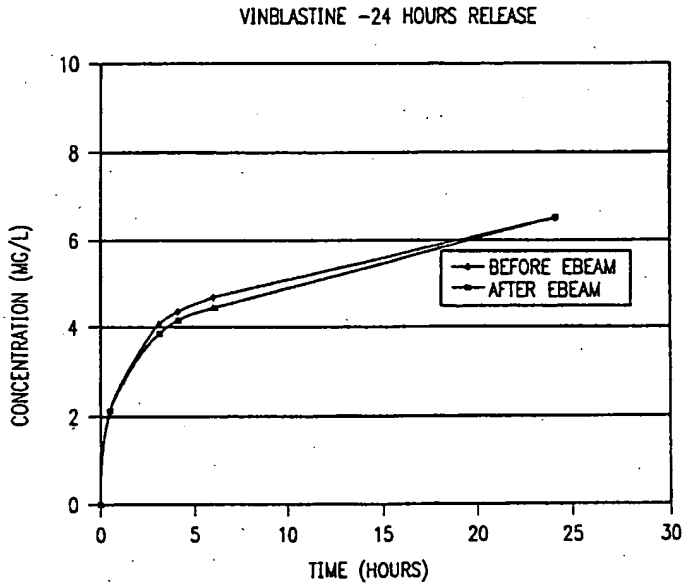
(54) Title: BIOCOMPTABIBLE COATING



(57) Abstract: A coating for a prosthesis, for example a stent, and a composition for forming the coating is disclosed. The coating can serve as a primer, allowing substances, such as polymers, to be effectively secured by the prosthesis. Alternatively, the coating can serve as a reservoir, allowing for the local and sustained release of a therapeutic substance to biological tissues. The composition can be formed from an ethylene vinyl alcohol copolymer and a dimethylsulfoxide solvent, with or without a therapeutic substance. Alternatively, the composition can be formed from an ethylene vinyl alcohol copolymer, a dimethylsulfoxide solvent, and a wetting fluid, with or without a therapeutic substance. The composition is applied to a surface of the prosthesis and essentially all of the dimethylsulfoxide solvent or dimethylsulfoxide solvent/wetting fluid is removed or allowed to evaporate to form the coating.

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A BIOCOMPATIBLE COATING

BACKGROUND OF THE INVENTION

Field of the Invention

This invention relates to a coating for implantable devices, such as an expandable intraluminal prosthesis, one example of which includes a stent. Moreover, the invention is directed to a composition for coating an implantable device.

Description of the Related Art

Percutaneous transluminal coronary angioplasty (PTCA) is a procedure for treating heart disease. A catheter assembly having a balloon portion is introduced percutaneously into the cardiovascular system of a patient via the brachial or femoral artery. The catheter assembly is advanced through the coronary vasculature until the balloon portion is positioned across the occlusive lesion. Once in position across the lesion, the balloon is inflated to a predetermined size to radially pess against the atherosclerotic plaque of the lesion for remodeling of the vessel wall. The balloon is then deflated to a smaller profile to allow the catheter to be withdrawn from the patient's vasculature.

A problem associated with the above procedure includes formation of intimal flaps or torn arterial linings which can collapse and occlude the conduit after the balloon is deflated. Moreover, thrombosis and restenosis of the artery may develop over several months after the procedure, which may require another angioplasty procedure or a surgical by-pass operation. To reduce the partial or total occlusion of the artery by the collapse of arterial lining and to reduce the chance of the development of thrombosis and restenosis, an expandable intraluminal prosthesis, one example of which includes a stent, is implanted in the lumen to maintain the vascular patency. Stents are scaffoldings, usually

the body of the stent during delivery and expansion of the stent, and an absolute lack of control of the release rate of the therapeutic substance from the stent.

Another proposed method involved the use of a polymeric carrier coated onto the surface of a stent, as disclosed in U.S. Patent No. 5,464,650 issued to Berg et al. Berg disclosed applying to a stent body a solution which included a specified solvent, a specified polymer dissolved in the solvent, and a therapeutic substance dispersed in the blend. The solvent was allowed to evaporate, leaving on the stent surface a coating of the polymer and the therapeutic substance impregnated in the polymer. Among the specified, suitable choices of polymers listed by Berg, empirical results were specifically provided for poly(caprolactone) and poly(L-lactic acid). The preferred choice of mutually compatible solvents included acetone or chloroform. As indicated by Berg, stents where immersed in the solution 12 to 15 times or sprayed 20 times. The evaporation of the solvent provided a white coating. A white coloration is generally indicative of a brittle polymeric coating. A brittle polymeric coating is an undesirable characteristic, since portions of the coating typically become detached during stent expansion. Detachment of the coating causes the quantity of the therapeutic substance to fall below a threshold level sufficient for the effective treatment of a patient.

Accordingly, it is desirable to provide an improved coating that is susceptible to expanding with a prosthesis without significant detachment from the surface of the prosthesis. It is also desirable for the polymer to be able to strongly adhere to the surface of the prosthesis, thereby preventing loss of the polymeric coating during prosthesis delivery. Other desirable features include, but are not limited to, a polymeric coating which allows for a significant control of the release rate of a therapeutic substance, a polymeric coating that can serve as an under-layer for substances which do not easily or effectively bind or adhere to the surface of the prosthesis, a polymeric solution which need not be applied excessively to the surface of the prosthesis to form a coating of a suitable thickness, and a polymeric solution that can be uniformly applied to the surface of the prosthesis.

solution. In this embodiment, the ethylene vinyl alcohol copolymer can constitute from about 0.1% to about 35%, usefully from about 12% to about 20% by weight of the total weight of the composition, the dimethylsulfoxide solution can constitute from about 59.9% to about 99.8%, usefully from about 79% to about 87% by weight of the total weight of the composition, and the therapeutic substance can constitute from about 0.1% to about 40%, usefully from about 1% to about 9% by weight of the total weight of the composition.

In accordance with another embodiment, sufficient amounts of a therapeutic substance or combination of substances are dispersed in the blended composition of the ethylene vinyl alcohol copolymer, the dimethylsulfoxide solution, and a wetting fluid. In this embodiment, the ethylene vinyl alcohol copolymer can constitute from about 0.1% to about 35%, usefully from about 10% to about 25% by weight of the total weight of the composition, the dimethylsulfoxide solution can constitute from about 19.8% to about 98.8%, usefully from about 49% to about 79% by weight of the total weight of the composition, the wetting fluid can constitute from about 1% to about 80%, usefully from about 5% to about 40% by weight of the total weight of the composition, and the therapeutic substance can constitute from about 0.1% to about 40%, usefully from about 1% to about 9% by weight of the total weight of the composition.

The composition can be applied to the prosthesis simply by immersing the prosthesis into the composition or by spraying the composition onto the surface of the prosthesis. The dimethylsulfoxide solution or the combination of the dimethylsulfoxide solution and wetting fluid is removed from the composition which is applied to the surface of the prosthesis. The copolymer, with or without the therapeutic substance, solidifies and adheres to the surface of the prosthesis. One technique for removing the dimethylsulfoxide solution or combination of the dimethylsulfoxide solution and wetting fluid includes allowing the components to evaporate to a substantial elimination, for example, by heating the prosthesis at a predetermined temperature for a predetermined duration of time.

BRIEF DESCRIPTION OF THE FIGURE

Figure 1A illustrates a fluid on a solid substrate having a contact angle Φ_1;

Figure 1B illustrates a fluid on a solid substrate having a contact angle Φ_2; and

Figure 2 is a plot showing elution profiles for stents with a coating of ethylene vinyl alcohol copolymer impregnated with vinblastine made according to Example 4.

DETAILED DESCRIPTION OF THE EMBODIMENTS

Composition

The embodiments of the composition are prepared by conventional methods wherein all components are combined, then blended. More particularly, in accordance to one embodiment, a predetermined amount of an ethylene vinyl alcohol copolymer (commonly known by the generic name EVOH or by the trade name EVAL) is added to a predetermined amount of a dimethylsulfoxide (DMSO) solvent at ambient pressure and under anhydrous atmosphere. If necessary, gentle heating and stirring and/or mixing can be employed to effect dissolution of the copolymer into the DMSO solvent, for example 12 hours in a water bath at about 60° C.

Ethylene vinyl alcohol copolymer refers to copolymers comprising residues of both ethylene and vinyl alcohol monomers. One of ordinary skill in the art understands that ethylene vinyl alcohol copolymer may also be a terpolymer so as to include small amounts of additional monomers, for example less than about five (5) mole percentage of styrenes, propylene, or other suitable monomers. In a useful embodiment, the copolymer comprises a mole percent of ethylene of from about 27% to about 44%. Typically, 44 mole percent ethylene is suitable. As a general rule, an increase in the amount of the ethylene comonomer content decreases the rate that a therapeutic substance is released from the copolymer matrix. The release rate of a therapeutic substance decreases as the

examples of the wetting fluid include, but are not limited to, tetrahydrofuran (THF), dimethylformamide (DMF), 1-butanol, n-butyl acetate, and mixtures and combinations thereof. In this embodiment, the ethylene vinyl alcohol copolymer can comprise from about 0.1% to about 35%, usefully from about 10% to about 25% by weight of the total weight of the composition. The DMSO solvent can comprise from about 19.9% to about 98.9%, usefully from about 50% to about 79% by weight of the total weight of the composition. The wetting fluid can comprise from about 1 % to about 80 % , usefully from about 5 % to about 40 % by weight of the total weight of the composition. The specific weight ratio of the wetting fluid depends on the type of wetting fluid employed and the weight ratio of the ethylene vinyl alcohol copolymer and the DMSO solvent. More particularly, tetrahydrofuran used as the wetting fluid can comprise from about 1% to about 44%, usefully about 21% by weight of the total weight of the solution. Dimethylformamide used as the wetting fluid can comprise from about 1% to about 80%, usefully about 8% by weight of the total weight of the solution. 1-butanol used as the wetting fluid can comprise from about 1% to about 33%, usefully about 9% by weight of the total weight of the solution. N-butyl acetate used as the wetting fluid can comprise from about 1% to about 34%, usefully about 14% by weight of the total weight of the solution.

In accordance with another embodiment, sufficient amounts of a therapeutic substance or a combination of substances are dispersed in the blended composition of the ethylene vinyl alcohol copolymer and the DMSO solvent, without the wetting fluid. In this embodiment, the ethylene vinyl alcohol copolymer can comprise from about 0.1% to about 35%, usefully from about 12% to about 20% by weight of the total weight of the composition, the DMSO solvent can comprise from about 59.9% to about 99.8%, usefully from about 79% to about 87% by weight of the total weight of the composition, and the therapeutic substance can comprise from about 0.1% to about 40%, usefully from about 1% to about 9% by weight of the total weight of the composition. More than 9% by weight of therapeutic substance can adversely affect characteristics that are desirable in the polymeric coating, such as adhesion of the coating to the prosthesis. Selection of a specific weight ratio of the ethylene vinyl alcohol

fine particles. The mixing of the therapeutic substance can be conducted in an anhydrous atmosphere, at ambient pressure, and at room temperature such that supersaturating the therapeutic substance is not desired.

Exposure of the ethylene vinyl alcohol/DMSO composition or ethylene vinyl alcohol/DMSO/wetting fluid composition to the therapeutic substance is not permitted to adversely alter the substance's composition or characteristic. Accordingly, the particular therapeutic substance is selected for mutual compatibility with the blended composition. Therapeutic substances or agents can include, but are not limited to, antineoplastic, antiinflammatory, antiplatelet, anticoagulant, antifibrin, antithrombin, antimitotic, antiproliferative, antibiotic, antioxidant, antiallergic substances, and combinations thereof. Examples of suitable antineoplastics include paclitaxel and docetaxel. Examples of suitable antiplatelets, anticoagulants, antifibrins, and antithrombins include sodium heparin, low molecular weight heparin, hirudin, argatroban, forskolin, vapiprost, prostacyclin and prostacyclin analogues, dextran, D-phe-pro-arg-chloromethylketone (synthetic antithrombin), dipyridamole, glycoprotein IIb/IIIa platelet membrane receptor antagonist, recombinant hirudin, thrombin inhibitor (available from Biogen), and 7E-3B® (an antiplatelet drug from Centocore). Examples of suitable antimitotic agents include methotrexate, azathioprine, vincristine, vinblastine, fluorouracil, adriamycin, and mutamycin. Examples of suitable cytostatic or antiproliferative agents include angiopeptin (a somatostatin analogue from Ibsen), angiotensin converting enzyme inhibitors such as Captopril® (available from Squibb), Cilazapril® (available from Hoffman-LaRoche), or Lisinopril® (available from Merck); calcium channel blockers (such as Nifedipine), colchicine, fibroblast growth factor (FGF) antagonists, fish oil (omega 3-fatty acid), histamine antagonist, Lovastatin® (an inhibitor of HMG-CoA reductase, a cholesterol lowering drug from Merck), monoclonal antibodies (such as PDGF receptors), nitroprusside, phosphodiesterase inhibitors, prostaglandin inhibitor (available form Glazo), Seramin (a PDGF antagonist), serotonin blockers, steroids, thioprotease inhibitors, triazolopyrimidine (a PDGF antagonist), and nitric oxide. An example of an antiallergic agent includes Permirolast potassium. Other therapeutic substances or agents which may be

such as by spraying the composition onto the prosthesis or immersing the prosthesis in the composition. The addition of a wetting fluid leads to a consistent application of the composition which causes the coating to be uniformly deposited on the surface of the prosthesis.

After the composition is applied, the prosthesis can be heating by, for example, passing the prosthesis over a hot plate. The prosthesis should be exposed to the heat for a short duration of time, typically about 3 to 5 seconds. The temperature of the hot plate can be from about 55° C to about 65° C, typically about 60° C. Exposure of the prosthesis to the hot plate prevents the prosthesis from cooling at a rapid rate. Rapid cooling of the prosthesis may adversely affect properties that are generally desirable in a coating, such as elasticity. The polymer can be further exposed to heat treatment or cured for a predetermined duration of time, for example for about 6 hours. The heat treatment can be conducted generally at the same temperature range as the hot plate, for example from about 55° C to about 65° C, typically about 60° C. The heat treatment prevents formation of air bubbles in the polymeric coating.

The DMSO solvent or the combination of the DMSO solvent and wetting fluid is removed from the composition on the surfaces of the prosthesis by allowing the DMSO solvent or combination of the DMSO solvent and wetting fluid to evaporate. The evaporation can be induced by heating the prosthesis at a predetermined temperature for a predetermined period of time. For example, the prosthesis can be heated at a temperature of about 60° C to about 70° C for about 12 hours to about 24 hours. The heating can be conducted in an anhydrous atmosphere and at ambient pressure. The heating can, alternatively, be conducted under a vacuum condition. It is understood that essentially all of the DMSO solvent and the wetting fluid will be removed from the composition but traces or residues can remain blended with the copolymer.

plurality of coating layers onto the prosthesis. The application of each layer should be performed subsequent to the evaporation of the DMSO solvent or DMSO/wetting fluid and the drying of the copolymer of the previous layer.

In one embodiment, a layer or a second coating formed from a polymeric material, without a therapeutic substance, is deposited on the therapeutic substance impregnated copolymer coating. Suitable polymeric material can include, but are not limited to, polycaprolactone (PCL), poly-D,L-lactic acid (DL-PLA), poly-L-lactic acid (L-PLA), poly(lactide-co-glycolide), poly(hydroxybutyrate), poly(hydroxybutyrate-co-valerate), polydioxanone, polyorthoester, polyanhydride, poly(glycolic acid), poly(glycolic acid-cotrimethylene carbonate), polyphosphoester, polyphosphoester urethane, poly (amino acids), cyanoacrylates, poly(trimethylene carbonate), poly(iminocarbonate), copoly(ether-esters), polyalkylene oxalates, polyphosphazenes, polyiminocarbonates, and aliphatic polycarbonates, fibrin, fibrinogen, cellulose, starch, collagen, PARYLENE®, PARYLAST®, polyurethane, polyethylene, polyethylene teraphthalate, ethylene vinyl acetate, silicone, polyethylene oxide, and mixtures thereof.

In another embodiment, a layer or a second coating formed from essentially an ethylene vinyl alcohol copolymer, without a therapeutic substance, can be deposited on the therapeutic substance impregnated copolymer coating. The substance-free ethylene vinyl alcohol copolymer used as a second coating can comprise a mole percent of ethylene of from about 27% to about 44%. It is understood by one of ordinary skill in the art that ethylene vinyl alcohol copolymer may also be a terpolymer so as to include small amounts of additionally monomers, for example less than about five (5) mole percentage of styrenes, propylene, and other suitable monomers.

The second coating produces a membrane that reduces the rate of release of the therapeutic substance or substances from the impregnated ethylene vinyl alcohol copolymer, particularly therapeutic substances that are water soluble (e.g., heparin, rapamycin, and dexamethasone). If an ethylene vinyl alcohol copolymer is used as a rate reducing membrane, as a general rule, an increase in the amount of ethylene comonomer content of the second coating decreases the rate that a

delivery catheter is inserted either percutaneously or by surgery into the femoral artery, brachial artery, femoral vein, or brachial vein, and advanced into the appropriate blood vessel by steering the catheter through the vascular system under fluoroscopic guidance. A stent having the above described coating may then be expanded at the desired area of treatment. A post insertion angiogram may also be utilized to confirm appropriate positioning.

EXAMPLES

The embodiments of the invention will be illustrated by the following set forth examples which are being given by way of illustration only and not by way of limitation. All parameters such as, grams of ethylene vinyl alcohol copolymer, DMSO, wetting fluid, and therapeutic substance, temperature, duration of time, thickness of coating, and all other parameters and data are not be construed to unduly limit the scope of the embodiments of the invention.

Example 1

Multi-Link™ stents (available from Guidant Corporation) were cleaned by placement in an ultrasonic bath of isopropyl alcohol solution for 10 minutes. The stents were dried and plasma cleaned in a plasma chamber. An EVOH solution was made with 1 gram of EVOH and 7 grams of DMSO, making an EVOH:DMSO ratio of 1:7. The mixture was placed in a warm water shaker bath at 60° C for 24 hours. The solution was cooled and vortexed. The cleaned Multi-Link™ stents were dipped in the EVOH solution and then passed over a hot plate, for about 3-5 seconds, with a temperature setting of about 60° C. The coated stents were heated for 6 hours in an air box and then placed in a oven at 60° C, under vacuum condition, and for 24 hours. The coated stents were expanded on a 4.0 mm angioplasty balloon. The coatings remained intact on the stents. The coatings were transparent giving the Multi-Link™ stents a glossy-like shine.

Example 2

Multi-Link™ stents were cleaned by placement in an ultrasonic bath of isopropyl alcohol solution for 10 minutes. The stents were dried and plasma

balloon. It is predicted that the coatings will remain intact on the stents. The coatings will be transparent, giving the Multi-Link™ stents a glossy-like shine.

Example 4

Multi-Link™ stents were cleaned by placement in an ultrasonic bath of isopropyl alcohol solution for 10 minutes. The stents were dried and plasma cleaned in a plasma chamber. An EVOH solution was made with 1 gram of EVOH and 7 grams of DMSO, making an EVOH:DMSO ratio of 1:7. Vinblastine was added to the 1:7 EVOH:DMSO solution. Vinblastine constituted 2.5% by weight of the total weight of the solution. The solution was vortexed and placed in a tube. The cleaned Multi-Link™ stents were attached to mandrel wires and dipped into the solution. The coated stents were passed over a hot plate, for about 3-5 seconds, with a temperature setting of about 60° C. The coated stents were cured for 6 hours in an air box then placed in a vacuum oven at 60° C for 24 hours. The above process was repeated twice, having a total of three layers. The average weight of the coating was 0.00005 grams, with an estimated vinblastine concentration of 12 ug per stent. Some of the stents were sterilized by electron beam radiation. The sterilized and unsterilized vinblastine coated stents were tested for a 24 hour elution period by placing one sterilized and one unsterilized stent in 5 ml of phosphated saline solution (pH 7.4) at room temperature with rotational motion. The amount of vinblastine eluted was evaluated by High Performance Liquid Chromatography (HPLC) analysis. The results of this test are given below and plotted in Figure 2. The data indicates that electron beam radiation procedure does not interfere in the release of vinblastine from EVOH.

Example 5

Multi-Link™ stents were cleaned by placement in an ultrasonic bath of isopropyl alcohol solution for 10 minutes. The stents were dried and plasma cleaned in a plasma chamber. An EVOH solution was made with 1 gram of EVOH and 7 grams of DMSO, making an EVOH:DMSO ratio of 1:7. Cephalotaxin was added to the 1:7 EVOH:DMSO solution. Cephalotaxin constituted 5% by weight of the total weight of the solution. The solution was vortexed and placed in a tube. The cleaned Multi-Link™ stents were attached to mandrel wires and dipped into the solution. The coated stents were passed over a hot plate, for about 3-5 seconds, with a temperature setting of about 60° C. The coated stents were cured for 6 hours in an air box then placed in a vacuum oven at 60° C for 24 hours. The above process was repeated twice, having a total of three layers. The average weight of the coating was 0.00013 grams, with an estimated cephalotaxin concentration of 33 ug. The stents were sterilized by electron beam radiation. Cephalotaxin/EVOH coated stents and EVOH-coated control stents were implanted in the coronary arteries of 4 pigs, generally in accordance to the procedure set forth in "Restenosis After Balloon Angioplasty-A Practical Proliferative Model in Porcine Coronary Arteries" by Robert S. Schwartz, et al., Circulation 82(6):2190-2200, Dec. 1990, and "Restenosis and the Proportional Neointimal Response to Coronary Artery Injury: Results in a Porcine Model" by Robert S. Schwartz et al, J Am Coll Cardiol; 19:267-74 Feb. 1992. Results of the porcine artery study indicated that there was no significant difference between the uncoated, EVOH coated and cephalotaxin coated stents in the amount of neointimal proliferation resulting from arterial injury.

Example 6

Multi-Link Duet™ stents (available from Guidant Corporation) were cleaned by placement in an ultrasonic bath of isopropryl alcohol solution for 20 minutes, then air dried. An EVOH stock solution was made with 1 gram of EVOH and 7 grams of DMSO, making an EVOH:DMSO ratio of 1:7. The mixture was

temperature. Various co-solvents were examined to determine which co-solvent would promote a thicker coating. These co-solvents were THF, DMF, 1-butanol, and n-butyl acetate. The formulation for the co-solvents was as follows. Three grams of dissolved EVOH:DMSO solution was mixed with 0.9 grams of THF; three grams of dissolved EVOH:DMSO solution was mixed with 0.39 grams of DMF; three grams of dissolved EVOH:DMSO solution was mixed with 0.5 grams of 1-butanol; and three grams of dissolved EVOH:DMSO solution was mixed with 0.68 grams of n-butyl acetate. The cleaned Multi-Link Duet™ stents, attached to mandrel wires, were dipped into the solutions. The coated stents were passed over a hot plate, for about 3 to 5 seconds, with a temperature setting of about 60° C. The coated stents were heated in a forced air convection oven for 24 hours. A second layer of coating was applied to coated Multi-Link Duet™ stents and the stents were heated in the same manner as above. No difference was seen between the stents coated with the various co-solvents (e.g., greater weight of coating or physical appearance). All coated stents were transparent, giving the Multi-Link Duet™ stents a glossy-like shine. No webbing or bridging of the coating was seen between the struts of the coated Multi-Link Duet™ stents. The weight of the coatings was between 0.2 to 0.27 mg/stent.

Example 9

Multi-Link Duet™ stents are cleaned in an ultrasonic bath of isopropyl alcohol for 20 minutes, then air dried. An EVOH stock solution is made having an EVOH:DMSO ratio of 1:4. The mixture is placed in a warm water shaker bath at 60° C for 12 hours. The solution is mixed, then cooled to room temperature. A 9% by weight Dexamethasone solution is formulated as follows: 2.96 grams of the EVOH:DMSO solution is mixed with 0.29 grams of Dexamethasone, then 0.9 grams of THF is added. The cleaned Multi-Link Duet™ stents are attached to mandrel wires and dipped into the solution. The coated stents are passed over a hot plate, for about 3 to 5 seconds, with a temperature setting of about 60° C. The coated stents are cured in a forced air convection oven for 2 hours. A second layer of coating is applied and cured in the above manner. It is predicted that the

CLAIMS

What is claimed is:

1. A coating for a prosthesis, comprising an ethylene vinyl alcohol copolymer.

2. The coating of Claim 1, wherein said prosthesis is selected from a group of balloon-expandable stents, self-expandable stents, and grafts.

3. The coating of Claim 1, wherein said coating is made from a composition comprising:

(a) said ethylene vinyl alcohol copolymer constituting from about 0.1% to about 35% by weight of the total weight of said composition; and

(b) a dimethylsulfoxide solvent constituting from about 65% to about 99.9% by weight of the total weight of said composition;

wherein after said composition is applied to a surface of said prosthesis, said dimethylsulfoxide solvent is essentially removed from said composition on said prosthesis to form said coating.

4. The coating of Claim 1, wherein said coating is made from a composition comprising:

(a) said ethylene vinyl alcohol copolymer constituting from about 0.1% to about 35% by weight of the total weight of said composition;

(b) a dimethylsulfoxide solvent constituting from about 19.9% to about 98.9% by weight of the total weight of said composition; and

(c) a fluid constituting from about 1% to about 80% by weight of the total weight of said composition;

wherein after said composition is applied to a surface of said prosthesis, said dimethylsulfoxide solvent and said fluid are essentially removed from said composition on said prosthesis to form said coating of said ethylene vinyl alcohol copolymer carrying said therapeutic substance.

10. The coating of Claim 9, wherein said therapeutic substance is selected from a group of antineoplastic, antiinflammatory, antiplatelet, anticoagulant, antifibrin, antithrombin, antimitotic, antiproliferative, antibiotic, antioxidant, antiallergic substances, and combinations thereof.

11. The coating of Claim 9, wherein said fluid is selected from a group of tetrahydrofuran, dimethylformamide, 1-butanol, n-butyl acetate, and mixtures thereof.

12. The coating of Claim 9, wherein said fluid has a contact angle less than about 90°.

13. The coating of Claim 1, additionally comprising a heparin layer disposed on at least a portion of said ethylene vinyl alcohol copolymer.

14. A method of forming a coating onto a surface of a prosthesis, comprising the acts of:

(a) providing a composition comprising an ethylene vinyl alcohol copolymer and a dimethylsulfoxide solution;

(b) applying said composition to said surface of said prosthesis; and

(c) removing essentially all of said dimethylsulfoxide solution from said composition on said prosthesis to form said coating.

22. A coating for a prosthesis produced in accordance with the method of Claim 21.

23. The method of Claim 21, wherein said ethylene vinyl alcohol copolymer constitutes from about 0.1% to about 35% by weight of the total weight of said composition, said dimethylsulfoxide solution constitutes from about 19.9% to about 98.9% by weight of the total weight of said composition, and said fluid constitutes from about 1% to about 80% by weight of the total weight of said composition.

24. The method of Claim 14, wherein said composition additionally comprises a therapeutic substance and a fluid selected from a group of tetrahydrofuran, dimethylformamide, 1-butanol, n-butyl acetate, and mixtures thereof.

25. A coating for a prosthesis produced in accordance with the method of Claim 24.

26. The method of Claim 24, wherein said ethylene vinyl alcohol copolymer constitutes from about 0.1% to about 35% by weight of the total weight of said composition, said dimethylsulfoxide solution constitutes from about 19.8% to about 98.8% by weight of the total weight of said composition, said fluid constitutes from about 1% to about 80% by weight of the total weight of said composition, and said therapeutic substance constitutes from about 0.1% to about 40% by weight of the total weight of said composition.

27. The method of Claim 24, wherein said therapeutic substance is selected from a group of antineoplastic, antiinflammatory, antiplatelet, anticoagulant, antifibrin, antithrombin, antimitotic, antiproliferative, antibiotic, antioxidant, antiallergic substances, and combinations thereof.

34. A method for forming an ethylene vinyl alcohol copolymer coating on a surface of a prosthesis, comprising the acts of:

(a) providing a composition comprising an ethylene vinyl alcohol copolymer and a dimethylsulfoxide solvent;

(b) adding a fluid to said composition, wherein said fluid reduces the viscosity of said composition; and

(c) applying said composition, having said fluid, to a surface of a prosthesis; and

(d) removing essentially all of said dimethylsulfoxide solvent and said fluid from said prosthesis, wherein an ethylene vinyl alcohol copolymer coating is formed on said surface of said prosthesis.

35. The method of Claim 34, wherein said prosthesis is selected from a group of balloon-expandable stents, self-expandable stents, and grafts.

36. A coating for a prosthesis produced in accordance with the method of Claim 34.

37. The method of Claim 34, wherein said fluid is selected from a group of tetrahydrofuran, dimethylformamide, 1-butanol, n-butyl acetate, and mixtures thereof.

38. A coating for a prosthesis produced in accordance with the method of Claim 37.

39. The method of Claim 34, wherein said fluid has a contact angle less than about 90°.

40. A coating for a prosthesis produced in accordance with the method of Claim 39.

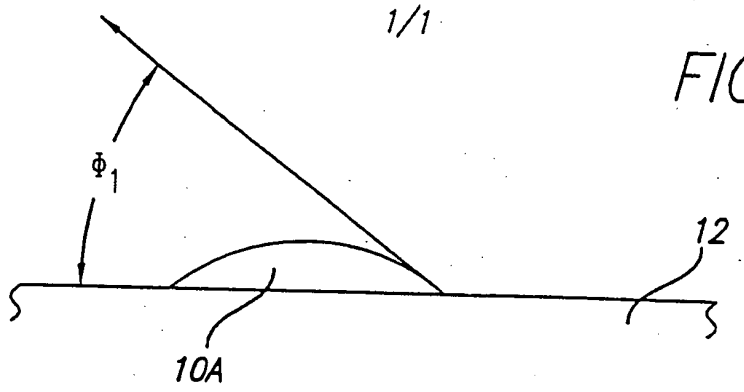

FIG. 1A

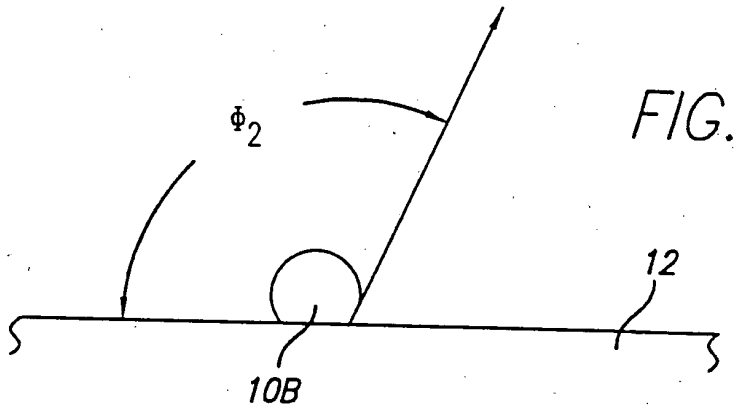

FIG. 1B

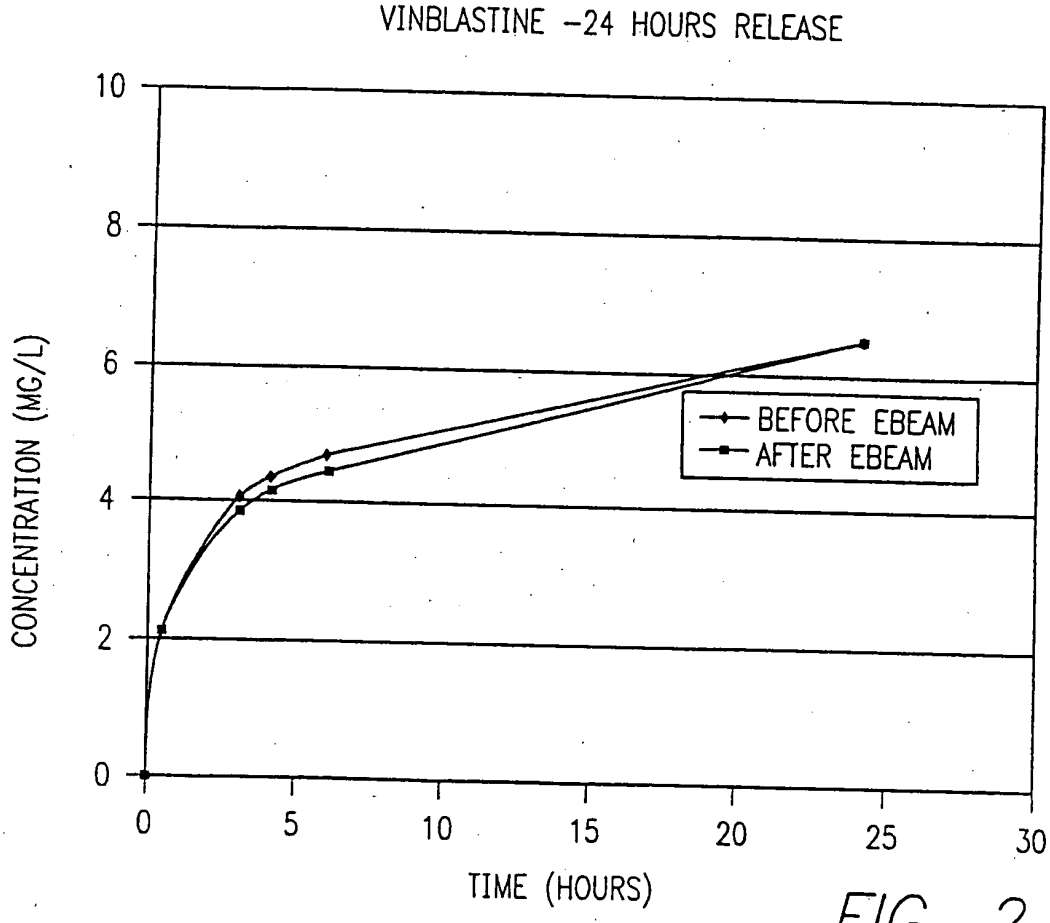

FIG. 2

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